RICHARDS, LAYTON & FINGER
A PROFESSIONAL ASSOCIATION
ONE RODNEY SQUARE
920 NORTH KING STREET
WILMINGTON, DELAWARE 19801
(302) 651-7700
FAX (302) 651-7701
WWW.RLF.COM

FREDERICK L. COTTRELL, III
DIRECTOR

DIRECT DIAL NUMBER
302-651-7509
COTTRELL@RLF.COM

April 16, 2007

BY ELECTRONIC FILING AND HAND DELIVERY

The Honorable Joseph J. Farnan, Jr.
United States District Court for
the District of Delaware
Federal Building
844 King Street
Wilmington, Delaware 19801

RE: ***The Procter & Gamble Company v. Teva Pharmaceuticals USA, Inc.,***
C.A. No.: 04-940-JJF

Dear Judge Farnan:

We represent The Procter & Gamble Company ("P&G") in the above-captioned case and write to respond to the April 9, 2007 letter to Your Honor (D.I. 105) from counsel for Teva Pharmaceuticals USA, Inc. ("Teva") discussing the Federal Circuit's recent decision in *Pfizer, Inc. v. Apotex, Inc.*, 2007 U.S. App. LEXIS 6623 (Fed. Cir. Mar. 22, 2007).

Teva would have the Court believe that the *Pfizer* case signals a change in the burdens of proof applicable to this suit. It does not.

Specifically, Teva contends that the Federal Circuit's decision in *Pfizer* supports the assertion made in its post-trial briefs, that, once the alleged infringer presents a *prima facie* case of obviousness, the burden of proving non-obviousness shifts to the patentee. As in its prior filings, in its letter, Teva selectively quotes language from the case law, and ignores the overall holding of the decision. Indeed, the Federal Circuit in *Pfizer* expressly rejected the proposition that Teva now advances to this Court, stating:

> Since we must presume a patent valid, the patent challenger bears the burden of proving the factual elements of invalidity by clear and convincing evidence. That burden of proof ***never*** shifts to the patentee to prove validity. The presumption of validity remains intact and the burden of proof remains on the challenger throughout the litigation, and the clear and convincing standard does not change.

Id. at *24 (citations omitted and emphasis added). The Federal Circuit went on to say that:

> It is true that once a challenger has presented a prima facie case of invalidity, the patentee has the burden of going forward with rebuttal evidence. But, all that means is that even though a patentee never must submit evidence to support a conclusion . . . that a patent remains valid, once a challenger introduces evidence that might lead to a conclusion of invalidity – what we call a prima facie case – the patentee would be well advised to introduce evidence sufficient to rebut that of the challenger.

Id. at *25 (citations omitted). The Federal Circuit, however, reiterated that "this requirement does not in substance shift the burden of persuasion, because the presumption of validity remains intact and ***the ultimate burden of proving invalidity remains with the challenger throughout the litigation***." *Id.* at *25-26 (citations omitted and emphasis added). Thus, "[t]he trial court has the responsibility to determine whether the challenger has met its burden by clear and convincing evidence by considering the totality of the evidence, including any rebuttal evidence presented by the patentee." *Id.* at *26 (citation omitted).

Teva would also have the Court believe that, in light of the Federal Circuit's holding in *Pfizer*, the inherent unpredictability of bisphosphonates is irrelevant to the Court's analysis of whether or not one of ordinary skill in the art in the mid-1980s would have had a "reasonable expectation of success." Again, Teva misreads the Federal Circuit's opinion, which stated merely that "obviousness cannot be avoided simply by a showing of ***some degree of unpredictability*** so long as there was a reasonable expectation of success" and that the expectation of success "need only be reasonable, not absolute." *Id.* at *38-39. In *Pfizer*, there was an admitted expectation of success but not a "guarantee." *Id.* at *39-40 (finding that the Pfizer scientist readily selected the besylate anion with the expectation, but no a guarantee, that it would, in fact, be successful). In contrast, as was amply demonstrated during the trial in this matter, in the bisphosphonate context, there was not merely "some degree of unpredictability"; rather, scientists in the mid-1980s (and even in the 1990s) were completely unable to predict whether one bisphosphonate compound would be effective or safe based upon its structural similarity to another bisphosphonate compound. *See, e.g.*, P&G's Proposed Findings of Fact ("PFF") (D.I. 99) ¶¶ 190, 198, 199, 203, 207-210. Thus, one of ordinary skill in the art in the mid-1980s with knowledge of 2-pyr EHDP and its properties would ***not*** have had any expectation of success, let alone a reasonable one, with respect to risedronate. *See, e.g.*, PFF ¶¶ 437-439.

Further factual distinctions between this case and the *Pfizer* case render the outcome in *Pfizer* inapplicable here:

- In *Pfizer*, scientists had to vary only one parameter and tried only seven different formulations before arriving at the patented formulation. *Pfizer*, 2007 U.S. App. LEXIS 6623 at *44. As proven at trial in this case, by contrast, when researchers attempted to identify a bisphosphonate that would achieve a suitable balance of antiresorption and

antimineralization, they examined numerous parameters that could be altered, including the length of the linking chain, substitutions on the pyridyl ring, and substitutions in the linking chain. *See, e.g.*, PFF 246-260. As a result, the P&G inventors and others working with them made hundreds of different bisphosphonates before stumbling upon risedronate. *See, e.g.*, PFF ¶¶ 172, 229, 231, 375. The Federal Circuit in *Pfizer* reiterated that, under such circumstances, there is unlikely to be a reasonable expectation of success, stating "'to have a reasonable expectation of success, one must be motivated to do more than merely vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.'" *Pfizer*, 2007 U.S. App. LEXIS 6623 at *42 (quoting *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed Cir. 2006)).

- The claimed product in *Pfizer* was merely a different salt of a previously-known compound. *Pfizer*, 2007 U.S. App. LEXIS 6623 at *9-10. In contrast, the invention at issue in this case is an altogether new chemical entity ("NCE"), risedronate. Indeed, the Federal Circuit expressly recognized the importance of this distinction to the "reasonable expectation of success" analysis when it stated, "These type of experiments used by Pfizer's scientists to verify the physicochemical characteristics of each salt are not equivalent to the trial and error procedures often employed ***to discover a new compound*** where the prior art gave no motivation or suggestion to make the new compound nor a reasonable expectation of success." *Pfizer*, 2007 U.S. App. LEXIS 6623 at *49 (emphasis added).

- The claimed product in *Pfizer* contained the same active ingredient as the prior art, and, as a result, there was no difference in the therapeutic effectiveness of the new formulation as compared to the prior art. *Id.* at *41, 51. In contrast, risedronate and the "prior art" 2-pyr EHDP are not the same active ingredient.[1] And, as the extensive evidence at trial demonstrated, 2-pyr EHDP and risedronate have vastly different therapeutic properties. *See, e.g.*, PFF ¶¶ 337, 342, 364, 371-383. For example, 2-pyr EHDP killed all of the test animals at the relatively low dose of 1.0 mg P/kg/day, while risedronate showed more than a 200% increase in bone volume at that dose. *See,* PFF ¶¶ 335, 336. The differences in structure thus significantly and unexpectedly affect the biological properties of the compounds.[2]

---

[1] Contrary to Teva's assertion, P&G most assuredly does dispute that the molecular structure of risedronate is "almost identical to that of 2-pyr EHDP." While the structures may appear similar when depicted two-dimensionally on paper, the actual three-dimensional molecular structures have important differences, which result in significant chemical and biological differences. *See, e.g.*, PFF ¶¶ 434, 435, 437-456.

[2] Indeed, the facts of the instant case are more similar to those in *Eli Lilly and Company v. Zenith Goldline Pharmaceuticals*, 471 F.3d 1369 (Fed. Cir. 2006). *Lilly* involved a new (Continued)

In short, Teva's reliance on the Federal Circuit's decision in *Pfizer* is misplaced. That decision only confirms that the asserted claims of the '122 patent are non-obvious, and that judgment should be entered for P&G.

Respectfully,

Frederick L. Cottrell, III (#2555)

FLC,III/afg
Enclosures

cc: Karen Pascale, Esquire (By Electronic Filing) (By Hand Delivery)
James Galbraith, Esquire (By Telecopy)
Vinita Ferrera, Esquire (By Telecopy)

---

chemical entity that was a homolog of similar structure to a prior art compound. In that case, the Federal Circuit stated: "This court will not ignore a relevant property of a compound in the obviousness calculus. When claimed properties differ from the prior art, those differences, if unexpected and significant, may lead to nonobviousness." *Lilly,* 471 F.3d at 1378 (citations omitted).

As in *Lilly,* in the present case, there was nothing in the '406 patent to suggest selecting 2-pyr EHDP as the lead compound to modify. In fact, the lethal toxicity of the compound described therein would teach away from selecting 2-pyr EHDP for modification. *See* PFF ¶¶ 408, 409.